A STUDY OF THE METABOLISM OF TWO ATYPICAL
CASES RELATED TO THE DEMENTIA
PRECOX GROUP.

By FRANCIS M. BARNES, Jr.,

*Assistant Physician and Director of the Clinical Laboratory, The Sheppard
and Enoch Pratt Hospital, Towson, Md.*

In the preceding paper the clinical condition of these two patients and the results of the examination of the blood have been reported. The details of the case histories and of the blood findings will not, therefore, be repeated here. To sum up briefly: in two individuals during their late twenties a psychosis develops, the onset and subsequent course of which in both cases are similar. The most striking features are the recurring attacks, during which varied grades of excitement and depression alternate. In the woman the excitement is still a most evident symptom, whereas in the man this element has almost entirely disappeared and its place taken by the marked depression (stupor) which in the woman now occurs only towards the end of the excited phase. Deterioration is evident in both patients. In the former paper and here they are considered as "atypical psychoses related to the dementia precox group and particularly to the katatonic variety, in which recurrent attacks, consisting of alternations between phases of varying length of excitement of a maniacal-depressive character, and stupor, persisting throughout a number of years have left the present condition of moderate deterioration noticeable principally in the affective sphere."

The blood examinations which were made on these two patients showed some interesting results but did not bring forth any proof of facts of importance from an etiologic standpoint. The coincidence of the changes in the number of leucocytes and in the temperature and pulse curves during a given phase as shown in the charts of the preceding paper suggested that a study of the metabolic processes during the different stages might afford additional knowledge of value to our understanding of these two cases. The rapidly alternating phases seemed to offer an excellent opportunity

for determining whether or not some variation from the normal of the metabolic processes might be present and bear some relation to the changes in the mental condition. Such variations have been noted to occur. Folin and Shaffer¹ have reported the results of a rather prolonged study of a case in which the phosphate excretion showed fluctuations in amount which paralleled the alternations in the mental state. It is to be regretted, perhaps, that the blood studies already reported could not have been carried out concomitantly with those of metabolism. Even if it had not been that the chemical work was suggested by the blood findings it is doubtful if there would have been sufficient time to carry out the two examinations over the same period. Although considerable time has elapsed between the two series of observations the condition of the patients has not changed materially and it seems that it may be assumed safely that the value of the work has not been vitiated in any way by this time interval and that the findings of several months ago are directly comparable with those made more recently during similar phases.²

PLAN OF THE WORK AND THE METHODS USED.

The original object of this work was to study under suitable known conditions the metabolism of these two patients. The analytical scheme used by Folin in his studies³ seemed to be quite satisfactory for the purpose and has been followed with but little change. As the urine work itself in the scheme is quite exacting the feces have not been analyzed. The diet proposed has several features to recommend it but principally because using this diet Folin has gathered together an amount of data concerning metabolism under both abnormal (mental diseases) and normal⁴ con-

¹ Folin and Shaffer: *The American Journal of Physiology*, 1902, VII, p. 135.

² During this interval between the blood and chemical work the present clinical laboratory was constructed and equipped and all methods to be used in this study were subjected to repeated controlled and checked experiments. These experiments have occupied the entire time for several months and were concluded only after the writer was satisfied that personal errors had been brought within permissible limits.

³ Folin: *The American Journal of Insanity*, 1904, LX, p. 699.

⁴ Folin: *The American Journal of Physiology*, 1905, XIII, p. 45.

ditions, which is available for comparison. The diets used in this work are as follows:

MILK AND EGG DIET.		STARCH DIET.	
Milk	500 ccm.	Pure arrow root, 400 grams, sodium	
Cream (18-25% fat).....	300 "	chloride, 6 grams, partially	
Eggs	450 gms.	digested with diastase in 1500	
Horlich's Malted Milk...	200 "	ccm. of water and served with	
Sugar	20 "	600 ccm. of cream.	
Sodium chloride	6 "	Water, extra.....	900 ccm.
Water, q. s. a. d.....	2,000 ccm.		
Water, extra.....	900 "		

These diets were made in the laboratory. All was given the patient before six o'clock each evening. To ensure as far as possible against all preventable losses and errors reliable special nurses were with these patients constantly during the entire time of the experiment.

The methods which have been used are all well-known and need no detailed description here. The amount of urine was measured in the customary cylinder; the specific gravity determined with an accurate hydrometer at 15 degrees centigrade; the reaction taken with ordinary litmus. Total nitrogen determined by the Kjeldahl method; phosphates by titration with uranium acetate with cochineal as indicator and chlorine estimated according to Volhard. Neutral sulphur, inorganic and ethereal sulphates, urea, ammonia, kreatinin, uric acid, acidity and indican determinations were all made according to the methods which have been devised by Folin.⁴ For several months prior to beginning the work on these two patients many experiments were carried out with all methods in

⁴ Folin has published a number of papers regarding these methods, of which only those describing the methods as finally adopted will be given here. Those described in the following articles are the ones used in this work. No variations have been introduced.

Sulphur and Sulphates. *The Journal of Biological Chemistry*, 1906, I, p. 131.

Urea. *Zeitschrift für physiologische Chemie*, 1902, XXXVI, p. 333.

Ammonia. *Ibid.* 1902, XXXVII, p. 161.

Kreatinin. *Ibid.* 1904, XLI, p. 223.

Uric acid. *Ibid.* 1901, XXXII, p. 552.

Acidity. *American Journal of Physiology*, 1903, IX, p. 265.

Indican. *Ibid.* 1905, XIII, p. 53.

order to determine their accuracy and uniformity. Experiments were made with both known standard solutions and with specimens of urine. In some instances as many as a hundred or more estimations have been made with one method. Sometimes a dozen duplicates have been carried through and seldom less than six. Exceedingly uniform results were obtained with each procedure and the accuracy comes well within the limits of technical error. The indican is not determined quantitatively. The urea method will not yield satisfactory results unless very closely watched while boiling with the magnesium chloride.

In the preparation of all solutions the greatest care has been exercised. This is true for those used in all titrations as well as for those used in testing the methods themselves. As in many of the determinations small quantities of urine are used inaccuracy in measurement may occur. To minimize such errors small amounts have been measured from pipettes graduated in 0.05 ccm. and larger ones from burettes graduated in 0.1 ccm. In view of the uniform results obtained by these methods duplicate analyses have been made only when some error seems to have occurred or when the results have differed widely from the similar determination of the preceding day. Such occasions have, of course, occurred and are not indicated in the tables. Where differences have been detected on a second determination either a third estimation is made for verification or the one which is considered the correct one is recorded. In several instances where the undetermined nitrogen has constituted an unusually large percentage of the total, the error is undoubtedly with the urea determination and has been detected too late for repetition. Aside from these errors I think that the figures represent as accurate results as may be expected.

ANALYTICAL RESULTS.

In Table I (Case I, No. 541) are given the figures for a period of thirty-four days (only thirty-three are shown here, as on December 27 part of the day's voiding was lost and the remainder not analyzed) divided into four sections according to the diet used. During the first no nourishment or water was taken, during the third the starch diet was employed, while during the second and fourth the milk and egg diet was given. The dietary change to

the last period was somewhat unfortunate as it was made at the time when the patient passed from the stuporous phase to the "normal" and any difference that may have occurred might have been masked. The experiment was discontinued because the patient objected strongly to the restrictions which it made necessary. He could not be persuaded to take the starch diet for a few days when "well," so that a comparison with the results obtained with this diet during the stupor could not be made. The first analyses represent the second day of the starvation period.

The clinical condition of this patient has not differed in general from that described in the foregoing paper. He entered upon one of his "abnormal" phases on the morning of December sixth. At first there was the usual degree of psychic elevation—continuous logorrhea, inaccessibility and irrelevancy. There was the accustomed rise in the curves representing the blood pressure, pulse and temperature, the last having begun to appear two days previously. After a short period of this excitement he subsided into his usual condition of stupor. On the fourteenth the temperature had again reached normal and with the exception of slight daily fluctuations remained there until January second, on which day he was up and dressed though somewhat stupid. The stuporous condition persisted with short periods of talkativeness interrupting until towards the end of the second week (December 20) when he began to indicate his wants by signs and gestures; a week later (December 29) he expressed a desire to get up and dress but by the time permission for this could be obtained he had again assumed his former semi-stuporous state. During the next few days he seemed to become progressively brighter and on January second was dressed and out of doors walking. On the following day, however, it was necessary to urge him to dress and after a morning spent in walking out of doors, playing pool, etc., he again became excited and remained so until evening. Coincident with this brief remission, during which time, however, he was not in his "normal" condition, there occurred similar fluctuations in the clinical curves as are seen during the main attack. Following this remission his condition was one of quite uniform stupor until the afternoon of January sixth when he reached his "normal" state. During the last few days of the experiment he was up and about,

TABLE I.—Case I.—No. 541.

Date.	Vol. in ccm.	Nitrogen in grams.						Ratios. 100 N ₂ .			Sulphur in grams SO ₃ .				Acidity, ccm. N/10.	Phosphates, Gms. P ₂ O ₅ .	Chlorine, Gms. NaCl.	Indican, Fehling's Solution = 100.	Remarks.
		Percentage of total nitrogen.						P ₂ O ₅ .	SO ₂ .	Cl ₂ .	Percentage of total sulphur.								
		Total.	Urea.	Ammonia.	Kreatinin.	Uric Acid.	Rest.				Total.	Neutral.	Inorganic.	Ethereal.					
Weight in Kg.	Sp. Gr. 15°C. 10.—																		
Dec. 8. '08	1240	16.28	12.85	0.58	0.88	0.36	1.62	35.12	61.15	2.81	0.62	2.04	0.15	821.28	5.72	9.96	23.8	2d day. Starvation.	
81.90	90	16.28	13.14	3.55	5.39	0.22	1.98	20.81	18.4	3.10	22.0	72.8	6.3	701.50	3.83	8.03	27.7	Stuporous, mute, etc.; in bed.	
9	890	16.28	13.81	0.74	0.74	0.22	1.29	20.81	18.91	3.10	0.52	2.45	0.14	701.50	3.83	8.03	27.7	Stuporous, mute, etc.; in bed.	
79.66	88	16.28	81.70	4.63	4.63	1.34	7.90	20.81	18.4	3.10	16.7	79.0	4.5	701.50	3.83	8.03	27.7	Stuporous, mute, etc.; in bed.	
10	660	12.99	10.29	0.77	0.49	0.18	1.81	21.41	18.71	2.48	0.37	1.94	0.12	733.39	2.78	1.94	2.0	Do. Albumin and casts since onset.	
77.56	84	12.99	79.20	5.92	3.80	1.00	10.00	21.41	18.71	2.48	16.4	80.8	5.0	733.39	2.78	1.94	2.0	Do. Albumin and casts since onset.	
11	590	12.63	9.45	0.90	0.48	0.13	1.80	17.20	19.76	2.47	0.41	1.97	0.19	723.58	2.15	0.93	0.0	Do.	
76.76	35	12.63	76.60	7.20	3.84	1.04	12.32	17.20	19.76	2.47	16.4	78.8	3.6	723.58	2.15	0.93	0.0	Do.	
12	560	12.56	8.96	1.02	0.54	0.18	1.86	14.83	20.38	2.57	0.40	2.08	0.11	588.16	1.87	0.86	0.0	Do.	
76.06	35	12.56	72.0	8.20	4.32	1.44	14.04	14.83	20.38	2.57	16.3	80.0	4.2	588.16	1.87	0.86	0.0	Do.	
13	520	12.07	9.54	0.74	0.53	0.18	1.08	8.77	19.83	2.43	0.34	2.02	0.08	487.50	1.07	0.71	0.0	Do. Bowels, 1.	
74.26	34	12.07	78.8	6.10	4.88	1.48	9.24	8.77	19.83	2.43	14.1	84.1	3.3	487.50	1.07	0.71	0.0	Do. Bowels, 1.	
14	530	11.81	9.13	0.80	0.45	0.17	1.28	12.92	17.6	2.07	0.29	1.70	0.08	509.90	1.52	0.42	Tr.	Do. 1860 ccm. water.	
73.80	34	11.81	77.8	6.77	3.80	1.44	10.70	12.92	17.6	2.07	13.8	80.9	3.8	509.90	1.52	0.42	Tr.	Do. 1860 ccm. water.	
8-14 Average	707.1 33.2	13.50	10.50	0.81	0.58	0.19	1.45	18.65	18.84	2.56	0.43	2.03	0.11	652.18	2.63	2.55	7.73	Starvation 1st Period.	
15	1090	22.59	19.15	1.21	0.64	0.35	1.24	14.34	15.66	3.56	0.34	3.05	0.17	701.09	8.26	1.04	62.5	Albumin and casts. 1860 ccm. water.	
76.06	29	22.59	84.7	5.85	2.53	1.64	5.68	14.34	15.66	3.56	9.44	84.7	4.7	701.09	8.26	1.04	62.5	Albumin and casts. 1860 ccm. water.	
16	1020	21.36	18.44	1.14	0.65	0.30	0.88	18.44	17.18	3.67	0.29	3.12	0.30	745.00	3.94	2.24	120.0	Albumin and casts. 560 ccm. water.	
77.60	31	21.36	86.5	5.30	3.04	1.40	3.80	18.44	17.18	3.67	7.1	86.6	8.3	745.00	3.94	2.24	120.0	Albumin and casts. 560 ccm. water.	
17	950	17.60	14.53	0.94	0.62	0.22	1.38	13.00	17.30	3.09	0.20	2.68	0.31	761.50	2.50	5.32	120.0	Stupor.	
79.66	30	17.60	82.1	5.80	3.60	1.20	7.8	13.00	17.30	3.09	6.4	83.2	10.0	761.50	2.50	5.32	120.0	Stupor.	
18	1200	17.51	14.28	0.90	0.60	0.20	1.57	15.36	17.04	2.99	0.27	2.44	0.28	791.36	2.70	11.87	110.0	Do.	
80.83	27	17.51	81.4	5.10	3.30	1.10	8.9	15.36	17.04	2.99	9.0	81.8	9.3	791.36	2.70	11.87	110.0	Do.	
19	1340	14.72	12.32	1.00	0.59	0.18	0.63	25.02	18.84	2.77	0.23	2.31	0.23	902.48	8.63	13.87	180.0	Do. Bowels, 1.	
81.00	25	14.72	53.8	6.8	4.00	1.20	4.2	25.02	18.84	2.77	8.2	82.5	8.2	902.48	8.63	13.87	180.0	Do. Bowels, 1.	
20	1160	14.16	11.05	0.73	0.52	0.19	1.07	25.77	19.98	2.88	0.23	2.83	0.27	741.0	8.65	11.83	160.0	Mute; indicates wants by gestures, etc.	
81.45	28	14.16	82.0	5.10	3.70	1.08	7.5	25.77	19.98	2.88	8.18	82.3	9.5	741.0	8.65	11.83	160.0	Mute; indicates wants by gestures, etc.	

21 81.45	1280	7.97	6.17	0.49	0.62	0.13	0.66	38.0	11.63	116.5	0.93	0.18	0.57	0.18	555.06	2.64	9.32	71.4	Stupor.
18	1820	6.23	8.59	0.45	0.63	0.13	0.63	38.18	12.99	201.7	0.98	0.18	0.35	0.15	462.28	1.91	10.56	55.5	Short period of logor-rhea last night.
22 81.45	1830	8.85	2.44	0.84	0.51	0.10	0.46	37.81	14.50	232.8	0.56	0.16	0.28	0.12	373.07	1.46	8.99	45.4	Stupor.
23 80.78	1840	8.19	63.80	8.83	13.34	2.63	11.9	48.2	16.59	140.2	0.53	0.14	0.28	0.11	355.84	1.54	4.48	25.0	Do.
24 81.23	1850	8.81	2.01	0.32	0.47	0.07	0.82	48.2	16.59	140.2	0.53	0.14	0.28	0.11	355.84	1.54	4.48	25.0	Do.
25	1860	3.81	2.17	0.37	0.61	0.06	0.88	42.84	19.33	244.0	0.75	0.23	0.37	0.16	398.96	1.61	9.28	29.4	Muteanswers questions by nodding head, etc.
26 81.00	1870	3.14	64.96	9.71	16.01	2.17	15.2	40.07	20.70	372.7	0.65	0.23	0.29	0.13	328.86	1.28	11.72	25.0	Mute. Bowels, 1.
28	1880	2.60	1.90	0.33	0.54	0.08	0.82	40.07	20.70	372.7	0.65	0.23	0.29	0.13	328.86	1.28	11.72	25.0	Mute. Bowels, 1.
29	1890	2.62	1.24	0.24	0.50	0.05	0.49	47.23	22.66	208.4	0.59	0.27	0.28	0.09	330.95	1.23	5.29	14.2	Brighter. Bowels, 1.
30	1900	2.88	63.10	11.25	18.30	2.77	14.5	47.23	22.66	208.4	0.59	0.27	0.28	0.09	330.95	1.23	5.29	14.2	Brighter. Bowels, 1.
31	1910	3.75	1.95	0.46	0.61	0.10	0.63	47.63	22.63	329.2	0.59	0.27	0.28	0.09	291.17	1.25	8.64	23.8	Talking in a. m.
32	1920	3.45	60.0	9.56	17.68	2.69	10.14	37.82	21.62	396.4	0.62	0.27	0.25	0.10	259.90	1.09	10.56	25.0	Talking at random in a. m. Bowels, 1.
33	1930	2.30	66.5	10.80	19.39	2.09	10.36	31.65	20.81	334.7	0.73	0.36	0.33	0.09	293.54	1.19	12.56	12.5	Do.
34	1940	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
35	1950	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
36	1960	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
37	1970	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
38	1980	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
39	1990	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
40	2000	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
41	2010	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
42	2020	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
43	2030	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
44	2040	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
45	2050	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
46	2060	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
47	2070	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
48	2080	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
49	2090	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
50	2100	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
51	2110	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
52	2120	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
53	2130	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
54	2140	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
55	2150	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
56	2160	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
57	2170	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
58	2180	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
59	2190	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
60	2200	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
61	2210	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
62	2220	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
63	2230	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
64	2240	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
65	2250	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
66	2260	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
67	2270	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
68	2280	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
69	2290	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
70	2300	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
71	2310	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
72	2320	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
73	2330	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
74	2340	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
75	2350	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
76	2360	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
77	2370	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
78	2380	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
79	2390	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
80	2400	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
81	2410	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
82	2420	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
83	2430	2.30	1.31	0.25	0.45	0.05	0.25	22.13	23.35	129.3	0.54	0.27	0.21	0.06	182.03	0.51	2.36	9.0	Out of doors; stupid. Bowels, 1.
84	2440	3.61	60.9	13.00	19.63	3.33	13.05	37.00	20.46	243.4	0.71	0.33	0.30	0.08	306.07	1.28	8.40	21.7	Do.
85	2450	2.30	1.31																

active most of the day, walking, playing games, reading, etc. During these last few days he complained much of the diet and maintained that he was very hungry. His weight on December sixth was 86.6 kilos and the seventh 83.3. Until the fourteenth of December, when he was allowed to have 1850 ccm. of water, he refused all offers of food and drink. During the starvation period the weight decreased very rapidly from 86.6 to 73.8 kilos. During this period albumin along with many hyalin and finely granular casts was present.⁶ Faint traces of albumin persisted for two days after taking the milk and egg diet. It has not been present excepting at the onset of an attack and that it is not entirely due to the withdrawal of food is shown by the fact that it was present in faint traces on January third, following the brief remission already mentioned. The presence of albumin has never been noted during the "normal" phase.

There is not much in the tables representing the results of the urinary examinations which is not quite obvious without especial reference here, although a few general points may permit of some further comment in this place. In Case I, Table I, during the starvation period there occurred a rapid fall in the weight and a gradual decrease in the amount of urine which became of a higher specific gravity. After the fourth starvation day the nitrogenous fractions maintained fairly constant amounts with the exception of the ammonia which increased somewhat both relatively and absolutely. Also, the undetermined nitrogen increased. The total acidity decreased only after having remained quite high for four days. The total sulphur decreased but little and this almost parallel with the total nitrogen. The percentage amount of neutral sulphur remained rather high, whereas the ethereal sulphates dropped in amount both absolutely and in percentage of the total sulphur. The indican disappeared very rapidly even in the presence of complete constipation from December fifth to thirteenth. Beginning the second period with the nitrogen-rich diet there is

⁶The albumin was neither removed from the urine before the total nitrogen determinations were made nor was it estimated by an accurate quantitative method (Esbach). This was an oversight which will explain, at least in part, the large percentage of undetermined nitrogen present during these days.

the marked increase in the amounts of the various nitrogenous bodies excreted. There is as marked coincident increase in the amount of urine following the excessive consumption of water at this time. This probable effect of the water on the nitrogenous excretion lasted only for the two days, but served to bring the averages for this period somewhat above the normal.⁷ It is noticeable that this effect of the water on the total nitrogen is more marked than it is upon the total sulphur and in consequence of this the $N_2 : SO_8$ ratio is lower on this day than at any other time while on this diet. The indican and chlorine values show the most decided changes in amounts. All of the changes are such as might be expected with such variations in food amounts and if the averages for this period are considered it will be seen that the various urinary constituents very soon reached amounts which are quite normal, with the exception of the indican, which is high.

The third period is interesting in the fact that it shows to what a great extent the distribution of the nitrogenous and sulphur fractions depend upon the total amounts of these two constituents present in the urine. The parallelism between the relative amounts of urea and inorganic sulphates on the one hand and between the kreatinin and neutral sulphur on the other is most striking. The other fractions show to a less extent the effect of this change in the absolute amounts of sulphur and nitrogen excreted. There is nothing unexpected in this behavior of these bodies⁸ and this diet was kept up for this length of time only in order to determine to what extent this change would affect the distribution of the component parts of the total nitrogen and sulphur. The indican alone showed results which were not to be looked for, that is, too high for this diet.⁹ The results of the fourth period require but a few words.

⁷ By "normal" here and in similar instances is meant the figures given as such by Folin in the American Journal of Physiology, 1905, XIII, pp. 62-63.

⁸ Folin: American Journal of Physiology, 1905, pp. 45, 66.

⁹ That more extensive effects were produced here than by Folin in his experiments is probably due to the fact that 300 ccm. additional cream were supplied with the diet. The very low results recorded on January 2 are about balanced by the high ones of the succeeding day and the apparent discrepancy is probably due to an unequal division of the 48 hours urine into two portions. The patient was continuously watched and the nurse is positive that none could have been lost.

Coincident with the change in his mental condition on the sixth there was discovered no change of moment in the urine. The indican alone shows a decided fall. As there occurred free evacuation of the bowels on January fifth and sixth it would seem that this decrease could very reasonably be explained by the removal of putrefactive material, and, further, that the excessive amount present on the preceding days was due to the accumulation of such material on which bacterial action might be exerted. No definite or constant relation is to be made out between the amount of ethereal sulphates present or the amount of indican as represented by these figures. Constipation seems to regulate within limits the indican formation; what it is that causes the sluggishness of the bowels is not known further than that during this stuporous phase there is a marked depression of body function in general. That an increased production of indol acting in a cumulative manner as a toxic agent may be the cause of the onset of the "attacks" does not seem probable. In the first place at the beginning of these observations the indican is low; secondly, during this attack and just preceding the transition from stupor to "normal" the amount of indican present does not seem to bear any relation to the mental state obtaining.

On looking over this entire series it is found that there is hardly a single feature which might be considered to show definitely an actual abnormality. Perhaps the neutral sulphur is slightly higher than would be expected but this can hardly be called abnormal. The various ratios show wider fluctuations than are conceded to be normal and particularly is this true of the nitrogen-sulphur ratio. It would seem, however, impossible to say just how far these variations were due to the changes in the diet and whether or not they would not entirely disappear in a few more days on a given diet.

With the second patient, the woman, a somewhat different condition was present. Her last "abnormal" period had extended over a somewhat longer time than was usual, about two months, and during this time the amount of nourishment taken was certainly insufficient. In this case the question of a more or less chronic general undernutrition must be kept in mind when considering the results of the urinary analyses. Her weight on Feb-

ruary fifteenth was 44.89 kilos (height 158 cm.), slightly more than half that of Case I (about 80 kilos, height 174 cm.). Further, during the experiment it was impossible to get this patient to take the full amount of special diet desired. Tube feeding was of no avail, as the food was regurgitated. Considering these several points the amount of the milk and egg diet given was only one-half that given to the man in the hope that this amount might be used uniformly throughout the experiment. It was impossible to use the starch diet in this case. During periods 1 and 2 (Table II) about 200 ccm. and during the remainder of the series 800 ccm. of water was given each day. Because of the differences in the diet the absolute amounts of the urinary constituents are not comparable in these two cases. The first analysis recorded represents the urine of the fourth day after beginning the diet. From February twentieth to twenty-fourth inclusive, the patient received the usual ward diet.¹⁰ The last analysis recorded (March fifth) represents but twelve hours excretion, from eight a. m. to eight p. m. on March fourth, the "abnormal" day. The figures on this day for the ammonia, uric acid and undetermined nitrogen are apparently incorrect and could not be re-determined for lack of material.

The clinical condition of the patient during the period of observation requires no especially detailed notice, as it has not differed materially from that described in the preceding paper and the curves of Chart III of that paper would fit very well the particular features existent while this present work was being carried on.

¹⁰ This patient presented so many difficulties in management, requiring the efforts of several nurses to care for her, that continuous observations could not be kept up and it was only attempted to carry out the work at the times of transition from one phase to another together with a sufficient number of days on either side of the changing point to make it possible to detect any variation in metabolism that might occur coincident with the mental deflections. This plan succeeded much better than was hoped and the different periods are indicated in Table II. With the beginning of the excitement on March 4 these difficulties became insurmountable and consequently the experiment was concluded abruptly after having obtained all of the urine secreted until 8 p. m. of that day. During the "abnormal" periods all urine was obtained by repeated catheterizations. The low results recorded on February 17 are explained by an unequal division of the excretion of two consecutive days.

TABLE II.—Case II.—No. 547.

Date.	Vol. in ccm.	Nitrogen in grams.						Ratios. 100 Ns.			Sulphur in grams SO ₂ .				Acidity, ccm. N/10.	Phosphates, Gms. P ₂ O ₅ .	Chlorine, Gms. NaCl.	Indican, Fehling's Solution = 100.	Remarks.
		Percentage of total nitrogen.						Cl ₂ .	SO ₂ .	P ₂ O ₅ .	Percentage of total sulphur.								
		Total.	Urea.	Ammonia.	Kreatinin.	Uric Acid.	Rest.				Total.	Neutral.	Inorganic.	Etheral.					
Feb. 15, '09	320	4.06		.386	.290	.080		37.68	23.96	138.67	0.973	.088	.779	.098	294.4	1.58	5.63	38.4	Stuporous and re-
44.89	.36			9.51	5.68	1.77						10.07	80.06	9.87					sitive.
16	325	4.29	3.40	.254	.250	.079	.31	28.21	25.52	135.24	1.095	.101	.834	.190	288.4	1.21	6.66	50.0	Short excited period
45.0	.35	79.23	5.92	5.58	1.84	7.23						9.22	76.16	14.61					during night.
17	265	3.65	2.80	0.24	.180	.087	.39	31.77	22.08	114.76	0.806	.077	.638	.091	276.6	1.16	4.19	38.4	Became "normal" 6.30
45.23	.36	76.69	6.57	4.93	1.01	10.68						9.55	79.15	11.29					p. m.
15-17 { Average	316.5 .356	4.00	3.10 77.96	.393 7.33	.340 5.47	.079 1.60	.35 8.95	32.55	23.85	136.22	.953	.093 9.61	.750 73.44	.115 11.93	288.5	1.30	5.49	42.3	1st Period. Stupor.
18	440	5.82	4.73	.380	.290	.078	.37	21.30	21.30	117.85	1.24	.110	.982	.148	308.0	1.24	6.86	45.4	In bed. "Normal.
45.23	.55	81.26	6.53	4.47	1.25	6.86						8.87	78.99	11.90					
19	465	5.62	4.32	.285	.282	.065	.70	30.60	22.06	95.89	1.24	.120	1.020	.100	363.4	1.72	5.89	22.7	Do.
45.34	.30	76.85	5.09	4.48	1.16	12.45						9.68	82.25	8.06					
20	510	5.83	4.69	.298	.240	.073	.59	24.57	21.30	108.58	1.24	.130	1.010	.100	285.6	1.43	6.32	50.0	Do.
45.56	.30	80.57	4.05	4.12	1.25	10.13						10.48	81.45	8.06					
19-20 { Average	471.5 .51	5.76	4.53 79.56	.300 6.23	.260 4.35	.070 1.53	.55 9.64	25.49	21.55	107.44	1.84	.120 9.67	1.00 84.19	.115 9.34	315.6	1.46	6.19	39.3	2d Period. "Normal."

TABLE II.—Case II.—No. 547.—Continued.

Date.	Vol. in ccm.	Nitrogen in grams.							Ratios. 100 N ₂ .			Sulphur in grams SO ₄ .				Acidity, ccm. N/10.	Phosphates, Gms. P ₂ O ₅ .	Chlorine, Gms. NaCl.	Indican, Fehling's Solution = 100.	Remarks.
		Percentage of total nitrogen.																		
		Total.	Urea.	Ammonia.	Kreatinin.	Uric Acid.	Rest.	Cl ₂ .	P ₂ O ₅ .	SO ₄ .	Total.	Neutral.	Inorganic.	Ethereal.						
Mch. 1. '00 47.03	1280 .16	7.37	6.20 84.07	.290 3.98	.225 3.05	.078 1.06	.57 7.73	30.10	21.15	76.34	1.56	.082 5.26	1.35 86.54	.130 8.33	409.36	2.22	5.63	50.0	In bed. "Normal."	
2 47.36	1000 .16	7.20	6.33 87.86	.297 4.08	.247 3.43	.091 1.26	.24 3.28	25.96	20.40	52.74	1.47	.108 7.35	1.22 82.98	.143 9.73	340.0	1.87	3.80	55.5	Do.	
3 47.03	1420 .13	7.20	6.20 86.60	.294 4.08	.290 3.19	.073 1.01	.21 2.97	24.96	19.85	56.13	1.43	.113 7.90	1.25 87.41	.070 4.90	289.68	1.80	4.26	45.4	Do.	
1-3 Average }	1233.3 .15	7.36	6.31 86.87	.293 4.03	.234 3.23	.081 1.11	.34 4.66	27.01	20.46	63.73	1.48	.101 6.83	1.27 85.64	.114 7.65	346.34	1.96	4.56	50.3	3d Period. "Normal."	
4 47.36	940 .19	7.13	6.20 86.92	.284 3.98	.281 3.94	.093 1.30	.27 3.79	22.15	20.61	63.23	1.47	.100 6.80	1.26 85.71	1.07 7.23	289.52	1.58	4.51	55.5	Excited, noisy, resis- tive. T _o a. m. = 100.2.	
5 (12 hrs.) 45.79	320 .28	3.64	3.15 86.53		.130 3.57			24.43	21.54	87.90	.794	.081 10.33	.064 84.66	4.86	121.60	.891	3.20	9.0	Excited, struggling, screaming, etc.	

The various phases during this cycle are indicated in Table II. On comparing Tables I and II one point is striking—no definite abnormalities are to be made out. This statement does not, of course, refer to the evident results of a condition of malnutrition which is pictured in Table II. The principal interest in this case seems to lie in the fact that we have here a condition of under-nutrition which affords a good opportunity of studying the metabolism in such a state. The amount of total nitrogen is low at first with a distribution of the various components somewhat similar to that observed when the total nitrogen is reduced by the starch diet as in Case I. This relative decrease in the urea with the attendant percentage increase in the other nitrogenous bodies does not here reach such striking extremes as is the case with the starch diet. With the slow increase in the total nitrogen the percentage distribution of the nitrogenous fractions gradually assumes what might be called a more normal aspect up until the end of the third period ending on March third. The undetermined nitrogen in this case never reached a large amount. The remarks on the nitrogenous bodies apply likewise to the total sulphur and its component parts but not to the same extent. It is to be remembered here that in proportion to the body weight the total amounts of nitrogen and sulphur excreted are not so excessively reduced from the normal and that consequently extensive disturbances of the usual distribution of their components would not be expected. When the ratios shown in Table II are examined it is seen that the P_2O_5 , SO_3 and Cl_2 in relation to the total nitrogen are high in amounts at first but gradually decrease as the nitrogen increases. In other words, the nitrogen increases in absolute amount relatively more rapidly than do these three urinary constituents.

With the increase in the various urinary constituents there is noted an increase in the weight. This cannot be attributed to this particular diet alone as it is always noted to occur during the "normal" phases. During the last "abnormal" period which persisted much longer than usual there was a considerable loss in weight which was not made up during this last "well" phase, so that she is still from five to seven or eight kilos below the average for her.

As the patient became excited at three a. m. on March fourth the urine analyzed on that day represents almost entirely that excreted on the last "normal" day of the preceding phase. If any change in metabolic function was to be expected to occur with any reference to the mental changes in this patient it would seem that it might reasonably be looked for here. Some such change as this may have occurred but is not demonstrable with the methods here employed. The only point noticeable, and that a small one, is that the kreatinin on this day was a trifle higher than it had ever been before in this patient. The results of the examination of the subsequent twelve hours' voiding offer no further help. Also, it might be noted that there was a decided loss in weight. So far as the work on this patient is concerned it has not shown that there is present any disturbance of the metabolism which bears any relation to the mental condition excepting the indirect one that during the "abnormal" phase undernutrition is evident. It was impossible to carry this examination further but it is a question whether further observations along this line would afford any facts of value from a psychiatric standpoint.

From the results of the study of the blood of these two cases it was concluded that the recurring hyperleucocytosis coincident with the changes in the mental state might be due to some form of intoxication which might find further expression in some discoverable disturbance of metabolism and it was thought that this present study might demonstrate the nature and extent of such metabolic disorder should it be present. The scheme of examination adopted for bringing about the solution of this problem has not been successful in accomplishing the desired object. This, however, does not mean necessarily that some such intoxication is not present until it is known that the methods here employed to detect it are efficient. Further work alone can clear up this point.